PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003013	12.07.2004	25.07.2003

International Patent Classification (IPC) or both national classification and IPC
G06F19/00, G01N33/68

Applicant
UNIVERSITY OF PLYMOUTH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/003013

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4,9,12,27
	No:	Claims	1-3,5-8,10,11,13-26,28-32
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	4,9,12,27
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	none

2. Citations and explanations

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/GB2004/003013

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1 : EP 0 800 085 A (ORTHO CLINICAL DIAGNOSTICS) 8 October 1997.

D2 : BENATTAR C ET AL: "EFFICIENCY OF ULTRASOUND AND BIOCHEMICAL MARKERS FOR DOWN'S SYNDROME RISK SCREENING. A PROSPECTIVE STUDY" FETAL DIAGNOSIS AND THERAPY, KARGER, BASEL, CH, vol. 14, no. 2, 1999, pages 112-117, XP000872100.

2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 20, 21 and 28-32 is not new in the sense of Article 33(2) PCT.

2.1 D1 discloses (the references in parentheses applying to this document):

A method of determining a likelihood of a fetus carried by a pregnant mother having a chromosomal abnormality (abstract; page 2; lines 19-28), a first biological parameter being suitable for screening said fetus for said chromosomal abnormality, the method comprising ("serum marker"; page 2, lines 31-39; page 3, line 55 - page 4, line 6):

receiving first data from a first stage of pregnancy of said mother, said first data comprising data representing a first value of said first biological parameter ("stage A", page 2, lines 31-39; "first trimester", page 4, lines 16-18, page 5, lines 14-17; Figure 1);

receiving second data from a second, later stage of said pregnancy, said second data comprising data representing a second value of said first biological parameter ("stage B", page 2, lines 31-39; "second trimester", page 4, lines 16-18, page 5, lines 14-17; Figure 1);

and determining likelihood data from said first and second data, said likelihood data representing the likelihood of said fetus having a chromosomal abnormality

(page 4, lines 16-28).

As a result, the subject-matter of claim 1 is not new within the meaning of Article 33(2) PCT.

2.2 Although claims 20 and 21 have been drafted as separate independent claims, they both contain all the features of claim 1 and moreover, claim 21 contains all the features of claim 20.

Since D1 discloses specification of Down's syndrome (DS) as a chromosomal abnormality (page 2, lines 10-15) and assaying samples obtained from pregnant women for the values of at least one screening marker (page 3, line 55 - page 4, line 8; page 5, lines 1-17), the subject-matter of claim 20 is not new in the sense of Article 33(2) PCT.

The additional feature of claim 21 defines determining the risk from the measurements taken at the first stage only. However, the functional link between this method step and the rest of the method is unclear. Nevertheless, since D1 discloses calculating the risk for Down's syndrome from the measurements obtained in the first trimester only (page 2, lines 15-18), the subject-matter of claim 21, so far as it can be understood, is not new over the disclosure of D1.

2.3 Independent claims 28 and 30 define computer programs with units corresponding to the steps of method of claims 1 and 20. Similarly, claims 31 and 32 define computer systems with means corresponding to the steps of method of claims 1 and 20. Since the subject matter of claims 1 and 20 is not new over the disclosure of D1 and since D1 also discloses a computer to implement its method (claim 9), the subject-matter of claims 28, 30-32 and claim 29 which defines a carrier with the computer program is also not new in the sense of Article 33(2) PCT.

3 Dependent claims 2-19, 22-27 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty or inventive step (Article 33(2) and (3) PCT).

3.1 The additional features of dependent claims 2, 3, 5-8, 10, 11, 13-19 and 22-26 are disclosed in D1 (see the corresponding passages cited in the International Search

Report).

3.2 Even though D1 does not explicitly calculate the correlation between the two values of the same marker taken at two different stages, such a correlation is implied in D1 (page 4, lines 40-56; Figure 1) since having high values at both stages or having low values at both stages is considered when making a decision on classification. In addition, the effect of compensation for variation claimed to have achieved by such correlations is mentioned in D1 (page 3, lines 1-55). Also, the same markers are eventually selected (hCG, PAPP-A, AFP, uE_3; page 4, lines 1-6; page 8, lines 6-11).

Moreover, it is well-known in the art of discriminant analysis that having a small within-class scatter (high correlation) and a large between-class scatter yields better classification performance. Therefore, no surprising unexpected effects are achieved by adopting features whose values are correlated in the two stages of measurements, so that a small within-class scatter is obtained within DS class and/or within unaffected class. This is greatly distinct from selecting features that behave the same way in both DS class and unaffected class (correlated markers), in which case the data points for the two classes will be unseparable (i.e. when the ellipses 10 and 20 in Figure 1b of the application collide).

Accordingly, ranges specified for correlations between the first and second measurements when selecting the markers as in claims 4 and 9 would be merely one of the several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill. As a result, the subject-matter of claims 4 and 9 does not involve an inventive step (Article 33(3) PCT).

3.3 Referring to claims 12 and 27, using data obtained from an ultrasound scan performed on mother during the first trimester when determining whether the fetus has chromosomal abnormality is well-known in the art as exemplified in D2 ("Nuchal translucency", abstract). It would be obvious to the person skilled in the art, to employ NT measurements from the first trimester in the risk calculations to get better detection rate and less false positives. Therefore, the subject-matter of said claims do not involve an inventive step within the meaning of Article 33(3) PCT.